Approach to a Patient of Bleeding Disorder

Dr. Salwa Bakr Hassan
Ass. Prof . & Consultant
Laboratory Hematologist

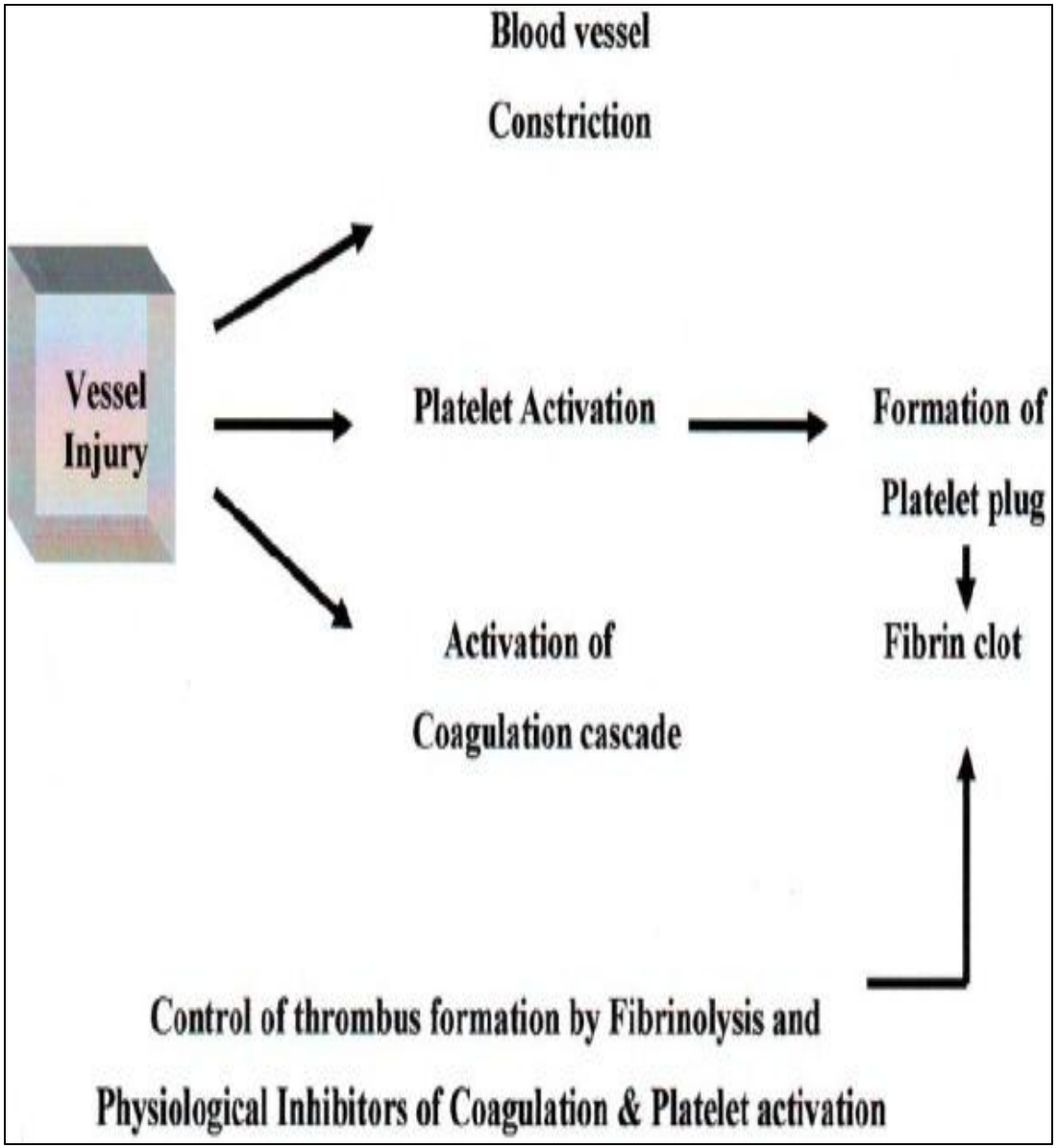
College of Medicine
PNU
2014-2015

Objectives

By the end of this lecture the student must be able to:

- Take a history of a patient with bleeding disorder
- Evaluate Clinically cases with bleeding disorders
- Enlist laboratory tests to evaluate cases with bleeding disorders

Normal Hemostasis



1ry Hemostasis:

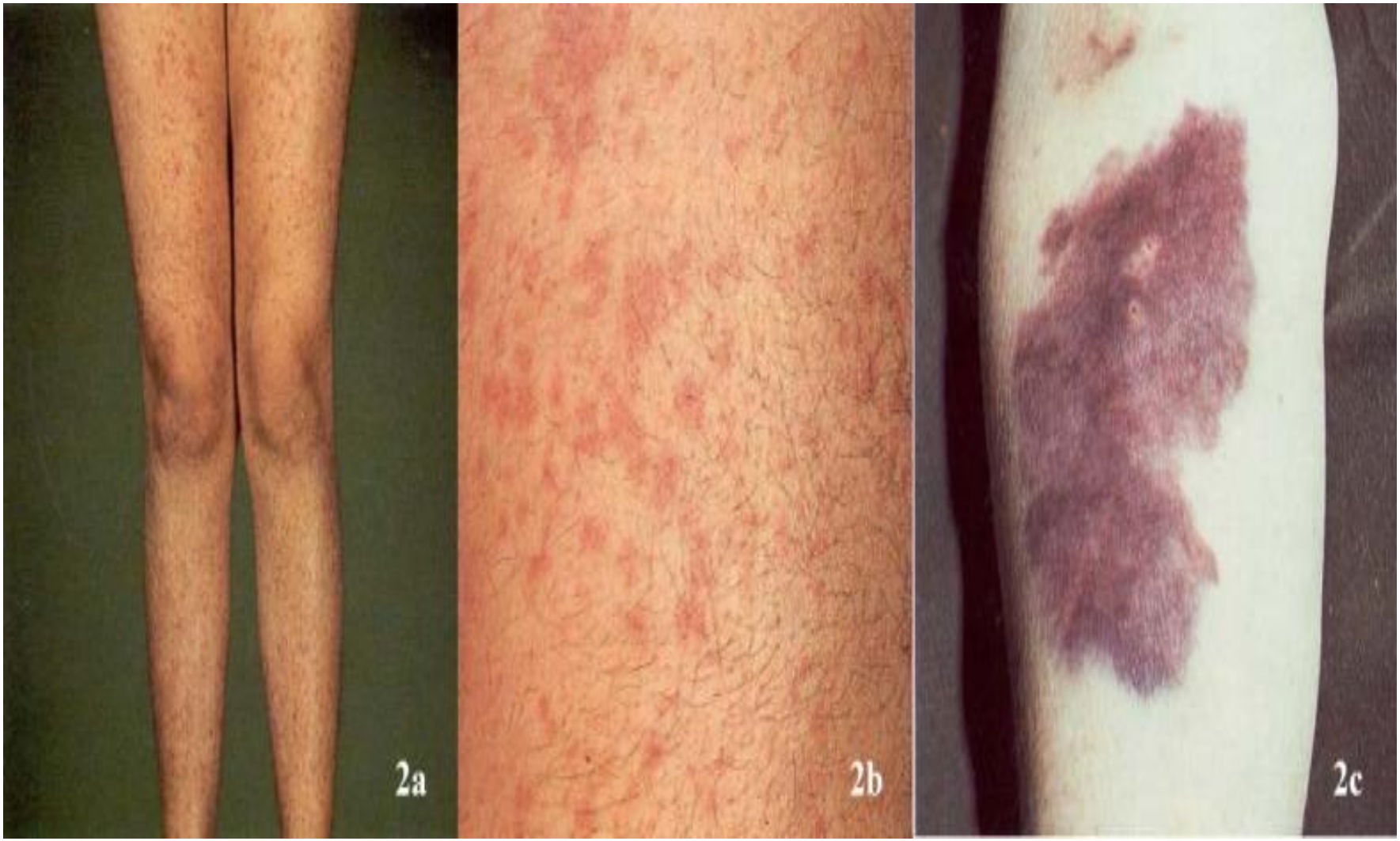
Requires normal vascular endothelium, platelets, vWF & fibrinogen.

2ry Hemostasis:

Requires normal *coagulation cascades*

The bleeding disorders results from :

- Abnormality of vessel,
- Platelets,
- or coagulation



Figures 2a and 2b shows scattered petechiae and purpura and **figure 2c** shows a large ecchymosis

Types of Bleeding Disorders:

1- Vessel interaction disorder (e.g.: vascular disorders , Thrombocytopenia, Platelet Function Defects, von Willebrand Disease) .

2- Coagulation disorders (e.g. Congenital as Hemophilia, Acquired as liver disease, Vitamin K deficiency, DIC, Factor VIII Inhibitor).

3-Hyperfibrinolysis (e.g.: Liver disease, Trauma, Major Surgery).

4-Congenital disorder of fibrinogen (e.g. Afibrinogenemia, Hypofibrinogenemia, Dysfibrinogenemia) .

Platelet Disorders

Causes of thrombocytopenia:

- Production failure
  - Congenital thrombocytopenia i.e. Wiscott-Aldrich syndrome
  - Pancytopenia (Aplastic anaemia, malignant infiltration)
- Increased peripheral consumption/ destruction
  - Immune (ITP, SLE, drugs)
  - non-immune (DIC, TTP, HUS)
- Splenic pooling (sequestration)
  - Hypersplenism
- Dilutional
  - Massive blood transfusion

Disorders of Platelet Function:

a) Inherited:

- Glycoprotein defect e.g. Glanzmanns thrombasthenia, Bernard Soulier syndrome and Von Willebrands disease.
- Granule defect e.g Grey platelet syndrome

a) **Acquired**: eg. aspirin ingestion, uraemia and in myeloproliferative disorders.

Disorders of the Coagulation Cascade

- **Inherited Bleeding Disorders** e.g. Hemophilia A (Factor VIII deficiency), Hemophilia B (Factor IX deficiency), Von Willebrand disease and congenital fibrinogen deficiency.

- **Acquired Bleeding Disorders** e.g. liver disease, vitamin K deficiency, DIC and anticoagulant therapy.

Disorders of vessels and supporting tissues

- Diagnosed by exclusion.
- If all investigations are found normal, the patient should be investigated for blood vessel wall abnormalities.
- Hess test +ve (capillary fragility test)

Blood vessel disorders :

- Hereditary e.g hereditary hemorrhagic telangiectasia and Ehlers-Danlos Syndrome, or
- Acquired e.g aging, Henoch-Schonlein purpura, scurvy, Cushing's syndrome and corticosteroid

Is the bleeding worth?;

RED FLAG

INFANT:

- Scalp bleeding at birth
- Bleeding from circumcision
- Delayed bleeding from umbilical cord
- Bleeding from blood sample
- Subcutaneous tissue/muscle swelling >3-4 cm
- Associated with immunizations during first year of life

SKIN BLEEDING:

- Skin bruise > 2 cm in diameter in size
- Located in upper extremities or trunk
- Petechiae located in face or extremities
- Associated with hematoma

MUCOSAL BLEEDING:

- Require medical intervention after dental work (suture, transfusion, iron therapy)

BLEEDING CHALLING:

- bleeding longer than 5-10 min after minor cut
- any bleeding require sutures
- poor wound healing and excessive scaring

NOSE BLEEDING:

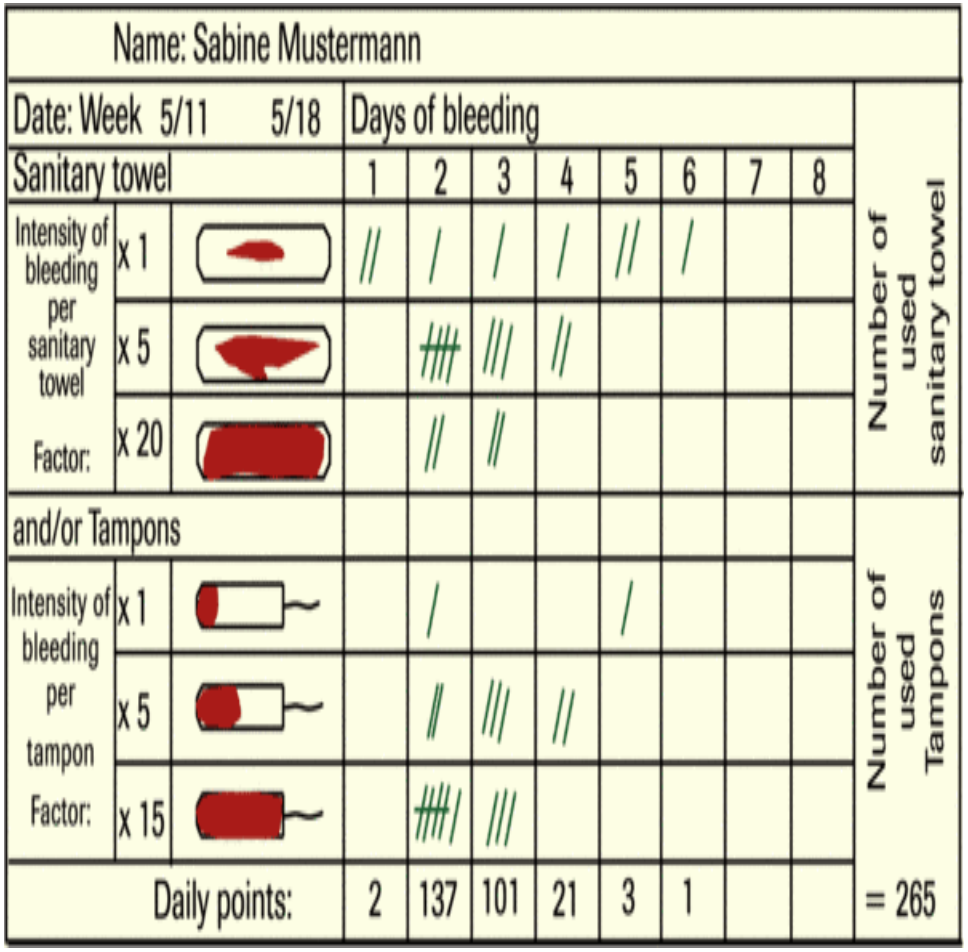
- Last longer that 10-15 min
- Require medical interventions (cauterization, transfusion, packing)

MENORRAHGIA:

- Menses >7 days duration
- > 1-2 days of heavy flow
- Blood clot >1'' in diameter

Menorrhagia; Bleeding Score Assessment

- 3 best predictor for abnormal menstrual blood flow:
  - Frequently changed pads/tampon that are completely socked with blood
  - Large clot> 1'' in diameter
  - Low ferritin level
- MENORRHAGIA SCORING SYSTEM:
- Pictorial blood assessment chart (PBAC) >100



Evaluation for the patient

- The establish the cause in a case of a bleeding patient, 3 key questions should be directed :
  - Local vs. systemic defect (nature of bleeding)
    - Location: single vs. multiple sites
    - Nature of bleeding , Severity: Spontaneous? Appropriate to trauma?,
  - Hereditary vs. acquired disorder
    - Age of onset
    - Family history (dominant/ recessive)
    - Associated systemic disease
    - Drugs
  - Pattern of bleeding :

Primary v.s. secondary hemostatic disorders.

Patterns of Bleeding Symptoms

	Platelet disorders	Coagulation factor disorders
Site of bleeding	Skin Mucous membranes (epistaxis, gum, vaginal, GI tract)	Deep in soft tissues (joints, muscles)
Petechiae	Yes	No
Ecchymoses “bruises”	Small, superficial	Large, deep
Hemarthrosis / muscle bleeding	Extremely rare	Common
Bleeding/after minor cuts	Yes	No
Bleeding after surgery or trauma	Immediate, usually mild	Delayed (1-2 days), often severe

Nature of bleeding

(a) Sites of bleeding (superficial /deep tissue)

may suggest where in the coagulation defect

(B) Severity of bleeding

(i) Spontaneous bleeding usually, is seen in severe bleeding disorders,

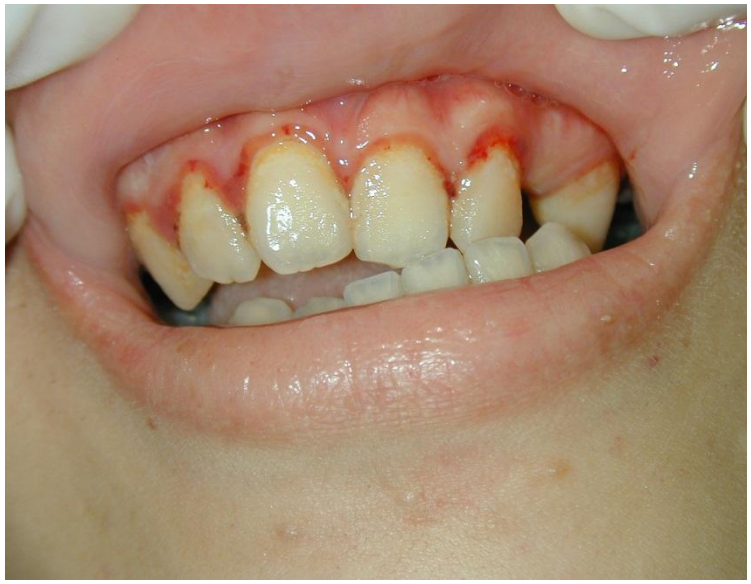
(ii) History of bleeding only after major trauma or surgery suggests a mild bleeding disorder,

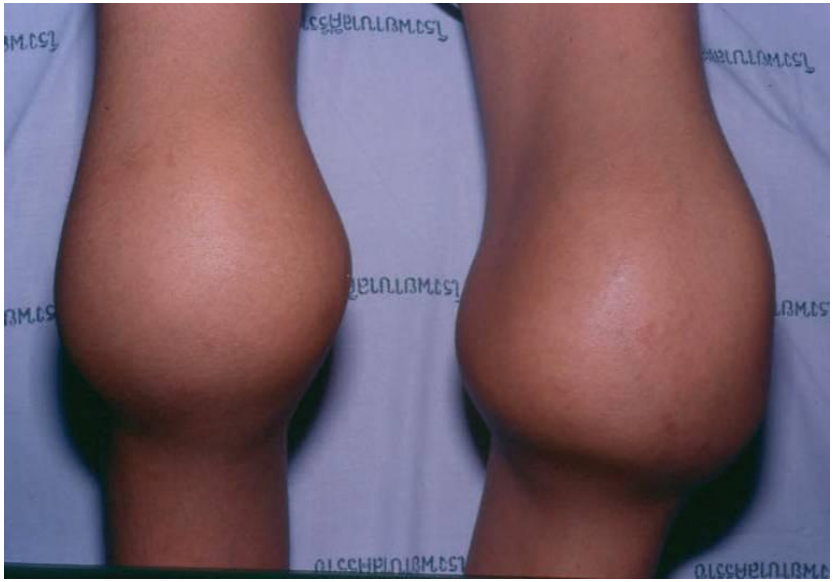
(C) Timing of episodes:

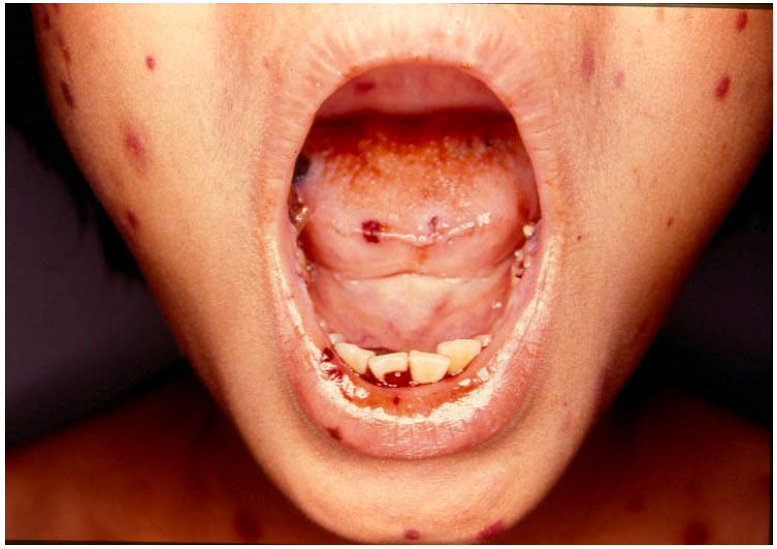
(i) Immediate : Bleeding uncontrolled from the onset suggests a defect in primary homeostasis**.**

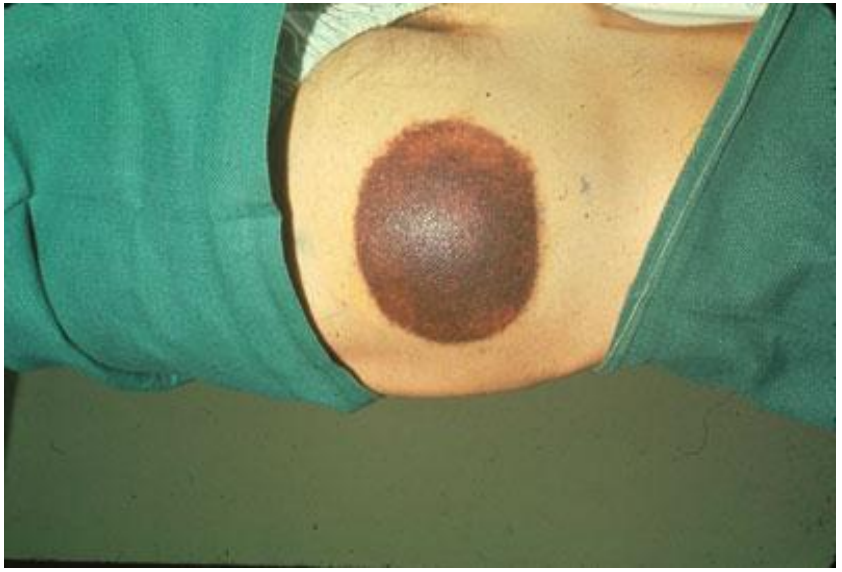
(ii) Delayed: Bleeding after apparent initial homeostasis are consistent with factor deficiency,

- A marked delay in bleeding after the initiating event is sometimes seen in **factor XIII deficiency**,





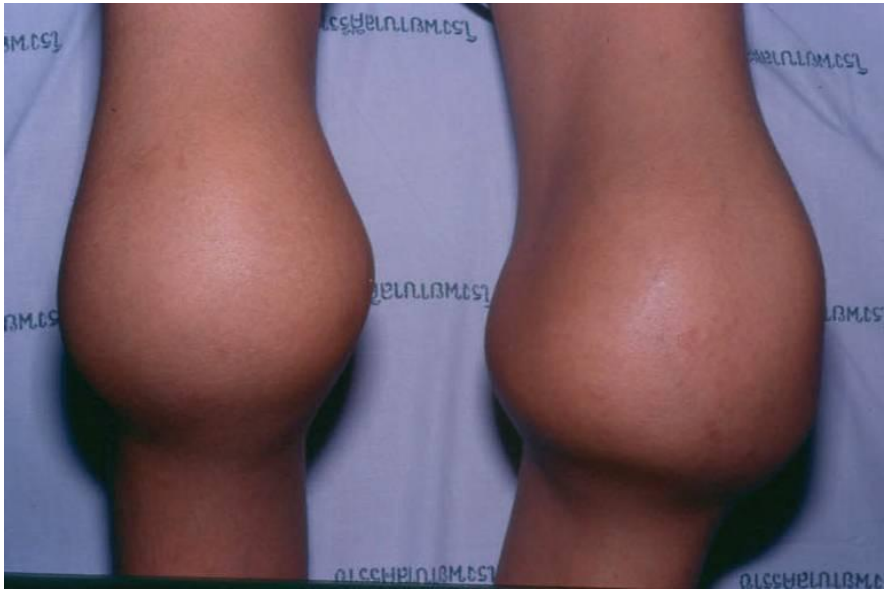


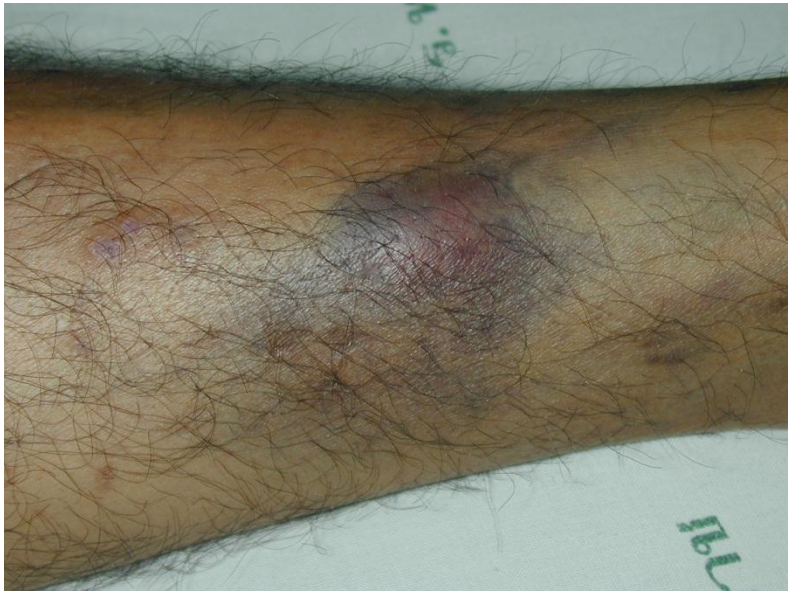


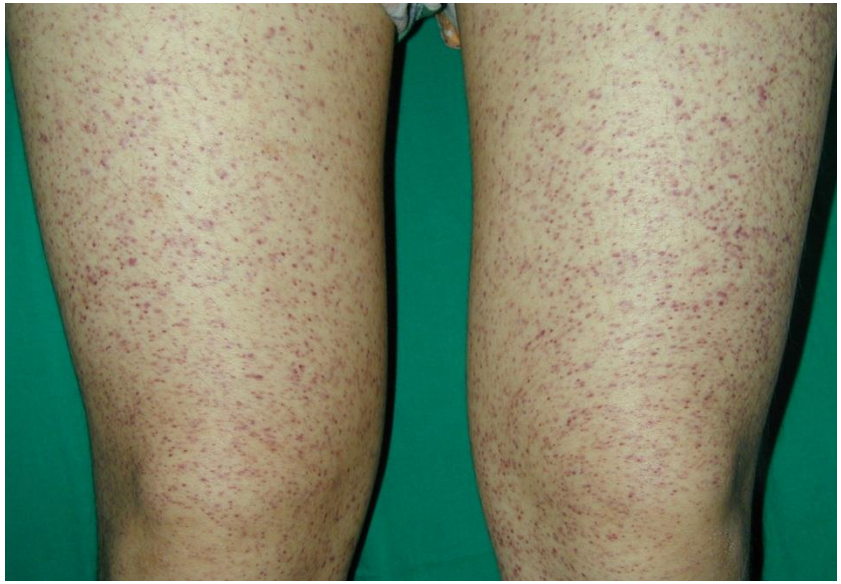
Primary Hemostatic defect

Secondary Hemostatic defect

What is the diagnosis?







Hereditary vs. acquired disorder

Clues to congenital disorders :

(a) Excessive bleeding initiated by common childhood trauma e.g; circumcision, tooth extraction.

(b) History of bleeding disorder in family and “when mode of inheritance can be determined:

- It may suggest specific diagnosis as well.
  e.g. X-linked in hemophilia A & B.
- Autosomal inheritance with low factor VIII C level suggests Von Willebrand disease.

Clues to acquired disorders :

- Exposure to potentially causative factors.
- onset of bleeding episodes: Patients giving history of bleeding tendency in recent times

Medical History

- Review of all medical conditions and their treatment can provide insight into possible nature of bleeding disorders e,g, :
- (a) **Liver disease, Vitamin K deficiency** seen in malnourished or hagic disease of newborn, antibiotics, **Uraemia**, disease abnormal protein, **Malignancy**, Acquire inhibitors.
- (b) **Immune mediated diseasea** seen in association with Systemic lupus erythematosus

  (SLE) and HIV infection,
- (c) Consumptive coagulpathy, **Disseminated Intravascular coagulation** (DIC) - most commonly seen in septicemia.

Medications

Careful review of all the medications is critical in evaluating a coagulation abnormality.

(I) Aspirin leading to platelet abnormality

(2) Over dosage of **oral anticoagulant** (warfarin)

(3) Incidental **Heparin** used for flushing Intravenous access lines (HIT),

(4) Acquired factor **inhibitors associated with medications e.g. penicillin**,

Evaluation of bleeding disorders

Can be divided into two parts clinical and laboratory:

I. Clinical Evaluation
- (a) Present history
- (B) Past history
- (c) Family history
- (d) Physical examination

2. Laboratory Evaluation
- (a) Screening tests
- (b) Specific tests

Clinical Evaluation of Bleeding Patients

- 85% of correct diagnosis can be made by a carful history taking and physical examination.

- A **meticulous history is essentially necessary in two circumstances.**
- (a) When clinical finding or past **medical history points to** a disorder of **homeostasis**.
- (b) In patients who do not show obvious homeostatic disorder but **who are scheduled for major surgery**.

Bleeding History Taking

Questions with the four “W's”, who, when, where and what are crucial.

- **Who**: who is the patient, sex, age, race, consanguineous marriage and family history of abnormal bleeding?
- **When**: when did the bleeding occur, i.e. onset of bleeding? Is it related to drug ingestion or any underlying disorder? Did it develop after surgery or trauma?
- **Where** : sites of bleeding, skin, muscle etc.
- **What**: description of the type of bleeding.

Questionnaire:

- Have you ever experienced a serious hemorrhagic complication **during or after surgical** procedure?
- Have you ever experienced excessive **vaginal bleeding** during or immediately after childbirth or perineal bleeding from an episiotomy?
- Have you ever experienced persistent **menorrhagia in absence of** fibroid or other uterine abnormality?
- Have you ever experienced brisk or prolonged bleeding after epistaxis or minor cuts or **exaggerated bruising after minor trauma**?
- Have you ever developed hemarthrosis, retroperitoneal hematoma **or soft tissue hematoma** in absence of major trauma?
- Have you ever experience **spontaneous** bleeding, **poor wound healing** or dehiscence of surgical wound?
- Has any member of your **family** experienced severe bleeding complication, perhaps **requesting transfusion of packed RBCs**?
- Do you have any **medical problems**?
- Do you take any **medications**?
- Have you noticed any **unusual rashes or easy bruisability** ?

II- Physical examination:

- To assess the sites and severity of the bleeding
- To evaluate whether the bleeding is part of a systemic illness, a local anatomical defect or a haemostatic disorder.
- To provide valuable clue as to where in the coagulation system is the defect

- Ecchymosis, Petechiae, epistaxis, deep soft tissue bleed, hemarthrosis, GI bleeding.
- Associated sign of “ Pallor, Jundice, fever, cachectic, Hepatosplenomegly, abdominal mass, ..”
- Abnormal elasticity of skin or hyper extensibility of joints should be sought as evidence of an hereditary connective tissue disorder associated with vascular bleeding. Telengiectasia should be noted.
- Look for physical signs and symptoms of diseases related to **capillary fragility**

III- Laboratory evaluation:

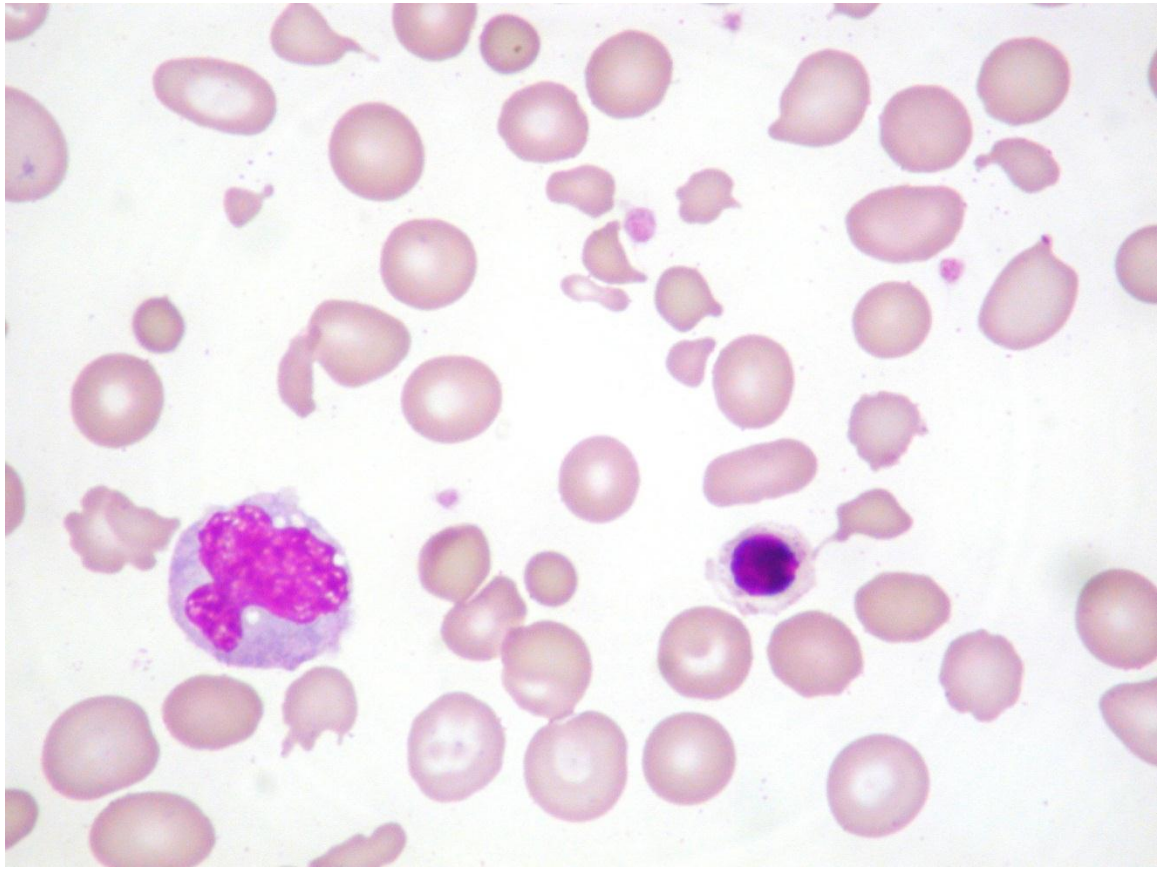
- Laboratory Studies: are guided by the history and physical finding in a patient
- However when no clues are available, a battery of appropriate tests often is the most expedient approach.

Screening tests of hemostasis:

(To distinguishing a platelet disorder from a coagulation defect)

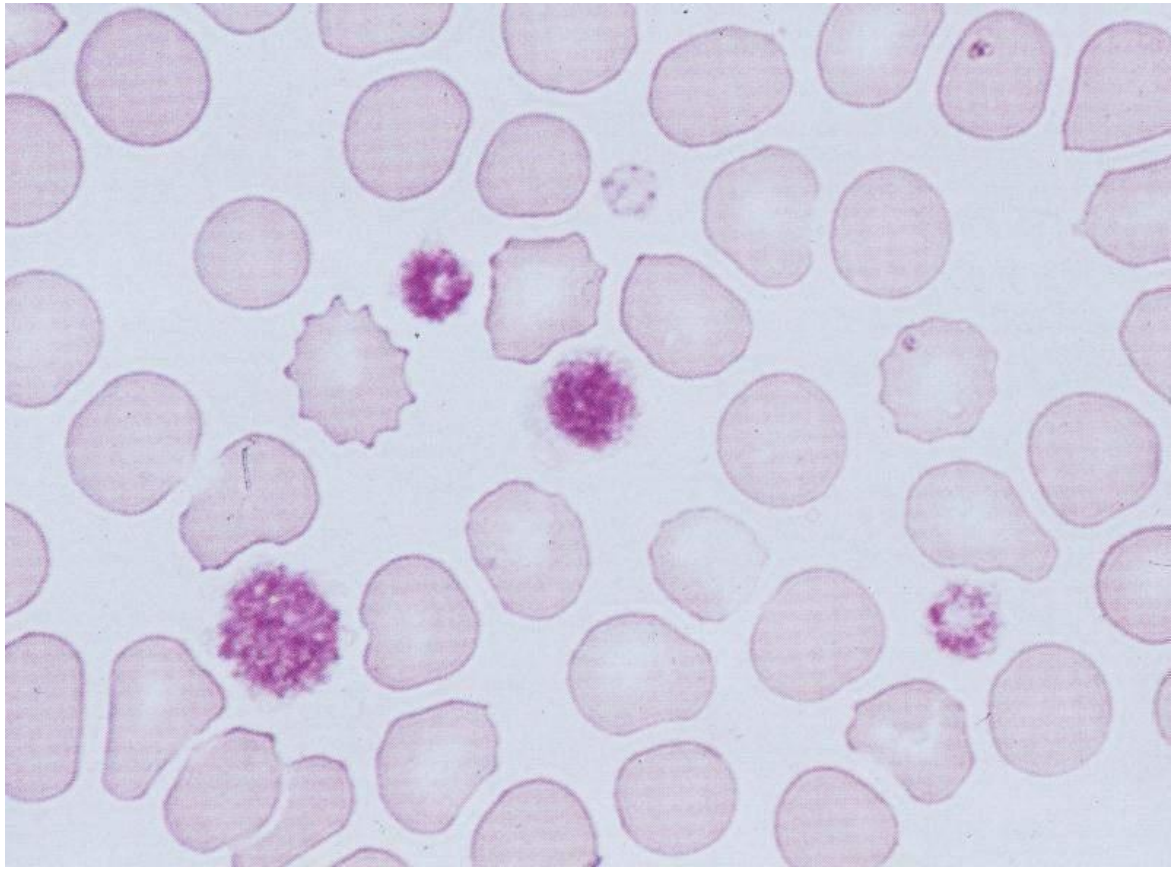
- Complete blood count (CBC) to assess platelet count,
- Peripheral blood smear examination,
- Prothrombin time (PT),
- Activated partial thromboplastin time (APTT),
- Thrombin time
- Bleeding time_or platelet function analysis (PFA-100)

Peripheral destruction: microangiopathic syndromes



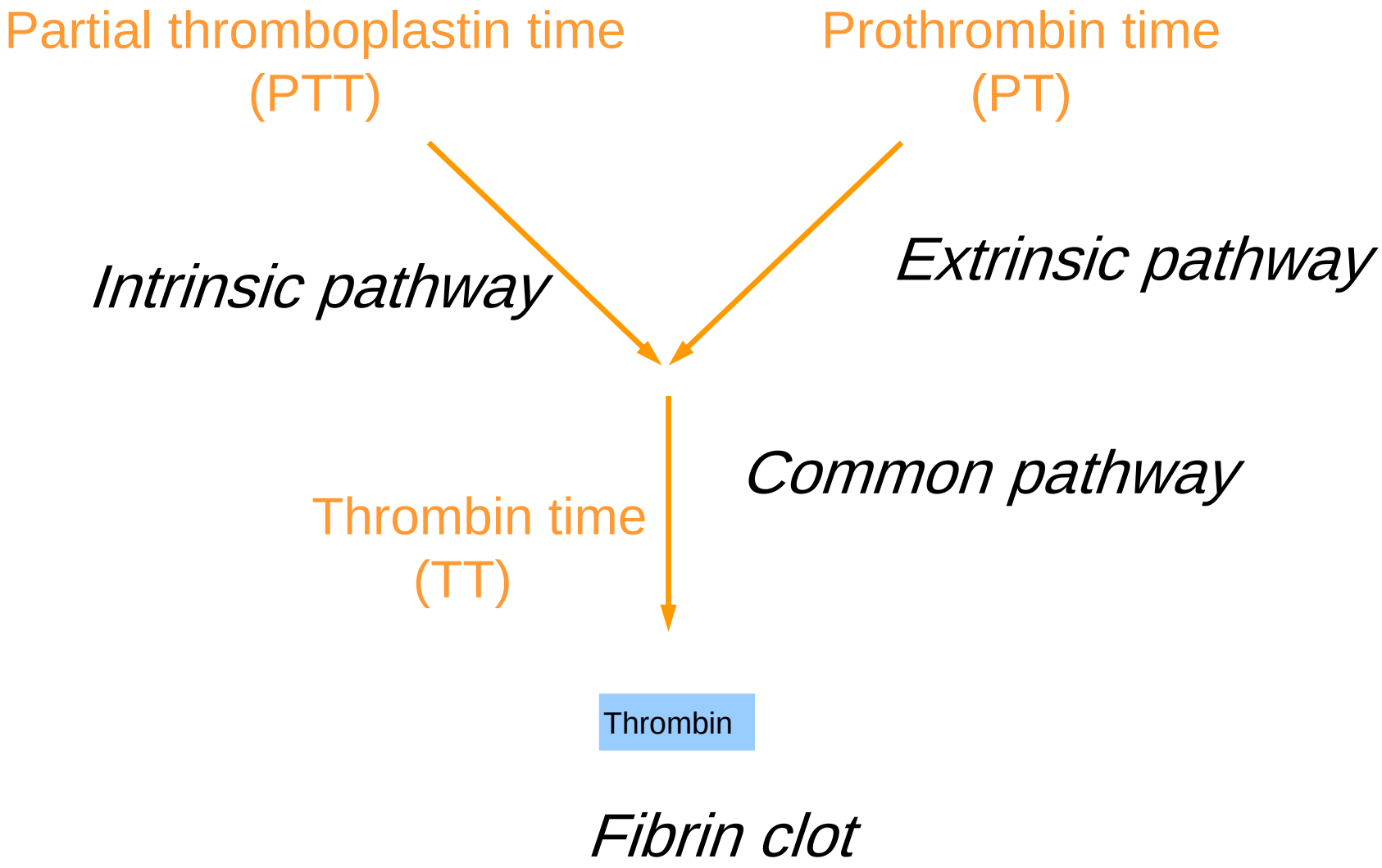
- E.g (DIC, TTP, HUS).
- TTP is an emergency condition
- Syndrome of a pentad (Fragmented RBCs, hemolytic anaemia, thrombocytopenia, renal failure, CNS involvement)

Hereditary Thrombasthenia ; Bernard-Soulier Syndrome



- Defective binding of VWF to platelet due to deficiency of GP-Ib receptor .
- On blood smear the platelet seen larger than normal.

Laboratory Evaluation of the Coagulation Pathways



Test	Possible conditions
Prolonged PT	Factor VII deficiency, early oral anticoagulation therapy
APTT	Deficiency of Factors VIII, IX, XI, XII, and Prekallikrien, Von Willebrand disease, Lupus anticoagulant
Prolonged PT and APTT	Deficiency of Factors V, X, II, oral anticoagulants, vitamin K deficiency, liver disease.
Prolonged PT, APPT and TT	Fibrinogen deficiency/disorder, liver disease, heparin.
Prolonged bleeding time or abnormal PFA result	Platelet function defect, Von Willebrand disease

Specific Tests

- Mixing studies
- Factor assays.
- Platelet aggregation test:

- Platelet aggregation defect with all aggregating agent (ADP, collagen, epinephrin, AA) except ristocetin =

GLANZMANN THROMBASTHENIA.

- Platelet aggregation defect with ristocetin only =

Bernard Soulier syndrome or **VWD**.

- Von Willebrand disease study (VW Factor assay, RcoF assay, RIPA)
- Low platelet count : (Bone marrow examination, Platelet antibodies, & Screening tests for DIC)
- Fibrinolytic assays : Euglobin clot lysis test.

Notes;

- If all investigations are found normal, the patient should be investigated for blood vessel wall abnormalities
- One should also be aware of conditions that may be associated with prolonged APTT but without a bleeding diathesis (F- XII deficiency).
- If all baseline-screening tests are normal then investigations for factor XIII deficiency and alpha 2-antiplasmin deficiency is demanded (clot solubility test).

Reference

- Chapters 25 - 26 , Essential Haematology by AV Hoffbrand, JE Pettit and PAH Moss, 6th Edition 2011, Blackwell Science